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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/029,905 | 12/21/2001 | Birgit Jung | 1/1177 | 5115 |

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| EXAMINER | |
|---|---|
| STEADMAN, DAVID J | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1656 | |

DATE MAILED: 10/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/029,905 | JUNG ET AL. | |
| | Examiner | Art Unit | |
| | David J. Steadman | 1656 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *15 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *12-15 and 19-59* is/are pending in the application.

4a) Of the above claim(s) *12-15 and 19-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *55-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.



SDO

## DETAILED ACTION

### *Status of the Application*

**[1]** The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1656.

**[2]** Claims 12-15 and 19-59 are pending in the application.

**[3]** Applicants' amendments to the claims, filed on 10/4/2004 and 7/15/2005, are acknowledged. The listing of the claims filed on 10/4/2004 fails to satisfy the requirements of 37 CFR 1.121 for the reason(s) set forth in the Office communication mailed 5/18/2005. The listing of the claims filed on 7/15/2005 replaces all prior versions and listings of the claims. It should be noted that even the claim listing filed on 7/15/2005 fails to provide a status identifier for claim 34. However, as claim 34 depends from claim 31, which is withdrawn, it follows that claim 34 is also withdrawn.

**[4]** Receipt of a sequence listing in computer readable form (CRF), a paper copy thereof, a statement of their sameness, a statement that no new matter has been added to the specification by the paper copy of the sequence CRF, and a statement directing entry of the substitute sequence listing into the specification, all filed on 1/31/2005, is acknowledged.

**[5]** Applicants' amendments to the specification, filed on 10/4/2004 and 7/15/2005, are acknowledged. The specification amendment filed on 10/4/2004 fails to satisfy the requirements of 37 CFR 1.121 for the reason(s) set forth in the Office communication

mailed 5/18/2005. The amendment filed on 7/15/2005 appears to correct these deficiencies.

**[6]** Applicants' arguments filed on 10/4/2004 have been fully considered and are deemed to be persuasive to overcome some of the objections and/or rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

**[7]** The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

### *Election/Restriction*

**[8]** Claims 12-15 and 19-54 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2/5/2004.

**[9]** Claims 55-59 are being examined on the merits.

### *Sequence Compliance*

**[10]** As noted in a previous Office action, this application fails to comply with the sequence requirements of 37 CFR 1.821 through 1.825. Applicants argue the sequence requirements are satisfied in view of the amendment to the specification and the submission of a substitute sequence listing. However, this is not persuasive as the corrected specification amendment filed on 7/15/2005 fails to amend the specification at

p. 26 to identify the sequence by a sequence identifier. Appropriate correction is required.

***Claim Rejections - 35 USC § 112, Second Paragraph***

**[11]** Claim(s) 57 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

**[a]** Claim 55 (claim(s) 56-59 dependent therefrom) is indefinite in the recitation of "reduces a chronic inflammatory airway disease" as it unclear as to what aspect of the disease is reduced. For example, is it the severity of the disease that is reduced? The occurrence? It is suggested that applicants clarify the meaning of the phrase "reduces a chronic inflammatory airway disease."

**[b]** Claim 55 (claim(s) 56-59 dependent therefrom) is incomplete as the active method steps do not necessarily achieve the desired result of determining whether a substance inhibits or reduces a chronic inflammatory airway disease. While the active method steps of (a) and (b) provide an indication as to whether the test substance modulates substrate phosphorylation, recognition, or binding, these active method steps fail to provide any indication as to whether the test substance can inhibit or reduce a chronic inflammatory airway disease. While it is acknowledged that the claim recites that a substance that activates substrate phosphorylation, recognition, or binding "*can be used* to inhibit or to reduce a chronic inflammatory airway disease" (italics added for

emphasis), the recited active method steps provide no indication that the activating test substance actually inhibits or reduces a chronic inflammatory airway disease.

**[c]** Claim 57 is indefinite in the recitation of "cellular effects caused by PAK2 kinase" as it is unclear from the claims and the specification as to scope of intended "cellular effects." It is acknowledged that the specification lists particular examples of "phenotyptic/cellular effects caused by PAK2" at pp. 25-28. However, these are merely representative examples and it is unclear as to other "cellular effects" that are intended as being encompassed by the term. It is suggested that applicants clarify the meaning of the term "cellular effects caused by PAK2 kinase."

***Claim Rejections - 35 USC § 112, First Paragraph***

**[12]** The written description rejection of claims 55-59 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below.

RESPONSE TO ARGUMENT: Applicants argue the rejection is overcome by amendment to limit the polypeptide to a "PAK2 kinase having an amino acid sequence as depicted in SEQ ID NO:4 or an equivalent, variant, mutant or fragment of the PAK2 kinase." According to applicants, the claims "recite sequence information and biological characteristics" of the genus of recited polypeptides.

Applicants' argument is not found persuasive. Initially, it is noted that MPEP 2111.01 states that "[d]uring examination, the claims must be interpreted as broadly as their terms reasonably allow." In view of the article "an" in the phrase "an amino acid sequence as depicted in SEQ ID NO:4," the examiner has broadly interpreted "a PAK2

kinase having an amino acid sequence as depicted in SEQ ID NO:4" as encompassing any PAK2 kinase polypeptide that comprises a fragment of as few as 2 contiguous amino acids of SEQ ID NO:4.

Regarding the genus of PAK2 kinase polypeptides and fragments thereof, while all members of the genus have a common function, *i.e.,* kinase activity, the members of the genus are widely variant with respect to their structures, particularly in view of the examiner's broad, but reasonable, interpretation of the phrase "a PAK2 kinase having an amino acid sequence as depicted in SEQ ID NO:4" as noted above. In this case, the specification discloses only a single species of the recited genus of PAK2 kinase polypeptides. While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus", it is also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus." Thus, because the structures of the members of the genus of PAK2 kinase polypeptides are widely variant, the single disclosed species of PAK2 kinase polypeptides, *i.e.,* SEQ ID NO:4, fails to represent the variation among the species. Similar reasoning applies to the genus of equivalents, variants, mutants and fragments of a PAK 2 kinase.

Thus, given the lack of description of a representative number of PAK2 kinase polypeptides or equivalents, variants, mutants, and fragments thereof, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

**[13]** The scope of enablement rejection of claims 55-59 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below.

RESPONSE TO ARGUMENT: Applicants argue the rejection is overcome by amendment to limit the polypeptide to a "PAK2 kinase having an amino acid sequence as depicted in SEQ ID NO:4 or an equivalent, variant, mutant or fragment of the PAK2 kinase." According to applicants, the claims "recite sequence information and biological characteristics" of the recited polypeptide. Applicants argue methods for determining biological activity of the equivalents, variants, mutants and fragments is well-known and undue experimentation is not required.

Applicants' argument is not found persuasive. The examiner maintains the position that the specification, while being enabling for a method for determining whether a substance is an activator or inhibitor of the kinase activity of SEQ ID NO:4, comprising the following steps: (a) contacting the polypeptide of SEQ ID NO:4 with a test substance in the presence or absence of a substrate of SEQ ID NO:4; and (b) measuring whether phosphorylation of the substrate of SEQ ID NO:4 in the presence of the test substance is inhibited or activated relative to phosphorylation of the substrate in the absence of the test substance, does not reasonably provide enablement for the full scope of the claimed method.

It is noted that claim 55 as amended is drawn to "[a] method for determining whether a substance inhibits or reduces a chronic inflammatory airway disease in which a macrophage is in a hyperactivated status due to down-regulated PAK2 kinase...wherein a substance which activates...is a substance which can be used to

inhibit or reduce a chronic inflammatory airway disease in which a macrophage is in a hyperactivated status due to down-regulated PAK2 kinase." However, the specification fails to provide any evidence that a substance that activates PAK2 kinase is an inhibitor of a chronic inflammatory airway disease or can reduce a chronic inflammatory airway disease in which a macrophage is in a hyperactivated status due to down-regulated PAK2 kinase. While the specification discloses evidence of a correlation between the level of PAK2 kinase mRNA and COPD (pp. 17-19), the specification fails to disclose a corresponding correlation between PAK2 kinase protein activity and COPD or any other chronic inflammatory airway disease. The ability to correlate the level of a protein or its activity based solely on the level of its transcript is highly unpredictable as evidenced by, *e.g.,* Greenbaum et al. (Genome Biol 4:117.1-117.8), Chen et al. (*Mol Cell Prot* 1:304-313), and Anderson et al. (*Electrophoresis* 18:533-537). In view of the teachings of these references, a skilled artisan would recognize that it is highly unpredictable as to whether the level of PAK2 kinase mRNA correlates with PAK2 kinase activity and/or whether PAK2 kinase level or activity correlates with COPD.

Regarding the scope of PAK2 kinase polypeptides, the examiner acknowledges the amendment to claim 55 to limit the polypeptide to a "PAK2 kinase having an amino acid sequence as depicted in SEQ ID NO:4 or an equivalent, variant, mutant or fragment of the PAK2 kinase." However, as noted above, the scope of claim 55 (claim(s) 56-59 dependent therefrom) encompasses most any PAK2 kinase polypeptide from any source and mutants and variants thereof having PAK2 substrate phosphorylation, substrate recognition, or substrate binding capability. While methods

for assaying for the substrate phosphorylation, recognition, or binding capability of a kinase polypeptide were known at the time of the invention, the specification provides no guidance for altering the PAK2 kinase of SEQ ID NO:4 with an expectation that the resulting polypeptide will maintain the desired activity/utility. As noted in a previous Office action – and undisputed by applicants – the functional effects of altering the amino acid sequence of a polypeptide are highly unpredictable and it was not routine at the time of the invention to screen all variants of a PAK2 polypeptide as encompassed by claim 55 for those that have PAK2 substrate phosphorylation, recognition, or binding capability. Thus, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the amount of experimentation required, it is the examiner's position that undue experimentation is necessary for a skilled artisan to make and use the entire scope of the claimed invention.

***Claim Rejections - 35 USC § 102***

**[14]** The rejection of claims 55-56 and 58-59 under 35 U.S.C. 102(b) as being anticipated by Benner et al. as evidenced by Database GenPept Accession Number Q13177 is maintained for the reasons of record and the reasons stated below.

RESPONSE TO ARGUMENT: Applicants argue that the specification discloses a correlation between COPD and PAK2 kinase. Applicants argue that because the claimed invention "does not deal with trivial assays for determining whether a substance

is an activator or inhibitor of PAK2 kinase," the reference of Benner et al. does not anticipate the claimed invention.

Applicants' argument is not found persuasive. Neither the preamble of the claim nor the limitation of "wherein a substance...due to down-regulated PAK2 kinase" carries "patentable weight." In this case, the preamble and the limitation of "wherein a substance...due to down-regulated PAK2 kinase have not been accorded any patentable weight as they merely recite the purpose of a process or the intended use of an identified test substance. Only active method steps (a) and (b) of claim 55 are considered by the examiner to have "patentable weight." As such, the methods of Benner et al., *e.g.,* contacting SEQ ID NO:4 with magnesium and substrate and measuring increased phosphorylation of the substrate, anticipates the claimed method.

**[15]** The rejection of claims 55-59 under 35 U.S.C. 102(b) as being anticipated by Lee et al. (PNAS 94:13642-13647) is maintained for the reasons of record and the reasons stated below.

RESPONSE TO ARGUMENT: Applicants argue that the specification discloses a correlation between COPD and PAK2 kinase. Applicants argue that because the claimed invention "does not deal with trivial assays for determining whether a substance is an activator or inhibitor of PAK2 kinase," the reference of Benner et al. does not anticipate the claimed invention.

Applicants' argument is not found persuasive. As noted above, neither the preamble of the claim nor the limitation of "wherein a substance...due to down-regulated PAK2 kinase" carries "patentable weight." In this case, the preamble and the

limitation of "wherein a substance...due to down-regulated PAK2 kinase have not been accorded any patentable weight as they merely recite the purpose of a process or the intended use of an identified test substance. Only active method steps (a) and (b) of claim 55 are considered by the examiner to have "patentable weight." As such, the methods of Lee et al., *e.g.*, contacting a cell endogenously expressing SEQ ID NO:4 with an anti-Fas antibody to induce apoptosis and measuring the cell extracts for kinase activity, anticipates the claimed method.

***Conclusion***

**[16]** Status of the claims:

- Claims 12-15 and 19-59 are pending.
- Claims 12-15 and 19-54 are withdrawn from consideration.
- Claims 55-59 are rejected.
- No claim is in condition for allowance.

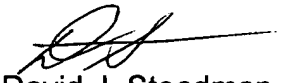
Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Thurs and alternate Fri, 7:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656